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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,299	09/22/2006	Kameron W. Maxwell	MITOS.004NP	4357

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EXAMINER	
RAE, CHARLESWORTH E	
ART UNIT	**PAPER NUMBER**
1611	

NOTIFICATION DATE	DELIVERY MODE
03/21/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/554,299	MAXWELL, KAMERON W.	
	Examiner	Art Unit	
	Charleswort Rae	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/13/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response without traverse to the restriction/election requirements, filed 12/19/07, electing invention I and 4-hydroxy-2,2,6,6-tetramethylpiperiden-1-oxyl as the compound species, surgery as the medical procedure species, and intravenous administration as the route of administration species, is acknowledged.

Applicant's statement that claims 1-23 read on the elected species.

Applicant's preliminary claim amendment filed 12/19/07 is also acknowledged.

For examination purposes, claims 16-23 are construed to be method of treatment claims.

Status of the Claims

Claims 1-23 are currently pending in this application.

Claims 24-31 are cancelled.

Priority

Receipt of applicant's certified copy of foreign priority application, received 10/24/05, is acknowledged.

Rejection under 101

35 USC 101 reads as follows

> Whoever invents or discovers any new and useful process, machine, manufacturer, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 16-23 are rejected under 35 USC 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e. results in a claim which is not a proper process claim under 35 USC 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. V. Brenner,* 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim rejections – 35 USC 112 – Second Paragraph

The following is a quotation of the second paragraph of 35 USC 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 17-23 provide for the use of a nitroxide in the preparation of a medicament to prevent a harmful effect of ischemia, but, since the claims do not set forth any active steps involved in the method/process, it is unclear what method/ process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Nonstatutory Obviousness-Type Double-Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-23 are rejected provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-25 of copending U.S. Patent Application No. 10/675,225 . Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are either anticipated by, or would have been obvious in view of the referenced claims.

In particular, reference claim 16 recites "[a] method of treating a patient, comprising topically applying a sufficient amount of a nitroxide radioprotector to prevent or treat harmful side effects caused by radiotherapy, wherein the nitroxide radioprotector is in solution in a solvent, and the solution is in the form of a low-residue

gel or a low-residue thickened liquid." Reference claim 17, for example, recites the identical compound as recited in instant claim 2.

To the extent that independent claims 1, 9, and 16 encompass "methods of preventing the harmful effect of ischemia," instant claims 1-23 are construed to read on any method of treatment employing the administering of the instant claimed nitroxide compounds as the term "preventing" or "prophylactic" are construed to mean the absolute absence of ischemia. Thus, the copending application makes obvious the instant invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims of the copending applications have not in fact been patented.

Claim Rejections – 35 USC 112 – First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for methods of reducing the harmful effects of ischemia comprising administering certain nitroxide compounds such as Tempol, does not reasonably provide enablement for preventing a harmful effect of ischemia in a human patient prior to the onset of ischemia by administering any and all nitroxide compounds to said patient. This is a scope of enablement rejection.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fd. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if its is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth in *In re Wands,* 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman* 230 USPQ 546 (BdApls 1986) at 547 the court cited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence or absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill of those in the art.

The invention in general relates to a method of treatment comprising identifying a human patient that is susceptible to ischemia and administering a sufficient amount of a nitroxide to prevent a harmful effect of ischemia in the human patient prior to the onset of ischemia.

The relative skill of those in the art is high, generally that of an M.D. or Ph.D. It is noted that the chemical and medical arts are generally unpredictable, requiring each embodiment to be individually assessed for chemical, pharmacologic, pharmaceutical, and clinical efficacy. The more unpredictable an area, the more specific enablement is necessary in order to satisfy the statue. (see *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970)).

Herfindal et la. teach that ischemia refers to a lack of oxygen secondatry to reduced perfusion (Herfindal et al. (eds.). Clinical Pharmacy and Therapeutics. 1992, pages 677-707, and 709; see page 677, first para). Herfindal et al. also teach that myorcadial ischemia is caused by an imbalance between oxygen supply and demand

usually as a result of atherosclerosis in the large epicardial coronary arteries; it may also occur as a consequence of either focal or generalized vasospasm of the major coronary arteries (page 677, first para.).

2. The breadth of the claims

The instant claims are relatively broad in scope. For example, claim 1 recites the term "identifying a human patient that is susceptible to ischemia" which given its broadest reasonable possible interpretation includes any and all living humans. Claim 1 also recite the term “a sufficient amount of a nitroxide to prevent a harmful effect of ischemia in the human patient prior to the onset of ischemia" which given its broadest reasonable possible interpretation is construed to mean the absolute absence of ischemia i.e. the instant method can prevent any and all ischemic events (i.e. all strokes, all myocardial infarctions, all angina) by administering any and all nitroxide to a patient identified as being susceptible to ischemia (see instant specification, page 8). The term "prophylactic or therapeutic amount of nitroxide to ameliorate a harmful effect of ischemia" recited in claim 9, and the term “prevent a harmful effect of ischemia through administration to a mammalian patient prior to the onset of ischemia” as recited in claim 16 are also very broad.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification discloses specific nitroxides (page 9-13). Example 1 describes a clinical study to determine the effect of Tempol on the prevention of cerebral ischemia (specification, page 12-13). However, Based on the instant disclosure, the applicant at best has provided specific direction or guidance only for a general method of treating a patient suspected of ischemia.

4. The quantity of experimentation necessary

In view of the uncertainty and unpredictability of in the medical art, coupled with the wide breadth of the claims, it is reasonable to surmise that the level of uncertainty in the art would require one skilled in the art to conduct more than routine experimentation in order to practice the claimed invention commensurate with the scope of the claims.

For the reasons stated above, claims 1-23 are rejected under 35 USC 112, first paragraph, for lack of scope enablement because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with the claims.

Claim rejections – 35 USC 102

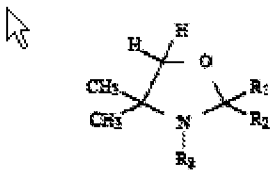
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-23 are rejected under 35 USC 102(b) as being anticipated by Mitchell et al. (US Patent 5,462,946).

The term "[a] method of treatment comprising identifying a human patient that is susceptible to ischemia" as recited in claim 1, and the term "identifying a patient scheduled to undergo a medical procedure involving a significant risk of ischemia as recited in claim 9 are construed to be inherent characteristics of the claimed method.

Mitchell et al. (US Patent 5,462,946) teach intravenous administration of compounds having the below formula, including 2,2,6,6-tetramethylpiperidine-1-oxyl (also known as TEMPO) and the elected compound, 4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl (also know as TEMPOL), for use as a protectant against oxidative stress in treating various conditions associated with oxidative stress such as reperfusion injury (see abstract; and col. 4, line 43 to col. 5, line 58):



wherein R_1 is $—CH_3$; R_2 is $—C_2H_5$, $—C_3H_7$, $—C_4H_9$, $—C_5H_{11}$, $—C_6H_{13}$, $—CH_2—CH(CH_3)_2$, $—CHCH_3C_2H_5$, or $—(CH_2)_7—CH_3$, or wherein R_1 and R_2 together form spirocyclopentane, spirocyclohexane, spirocycloheptane, spirocyclooctane, 5-cholestane, or norbornane, R_3 is —O. or —OH, or a physiologically acceptable salt thereof, and a pharmaceutically acceptable carrier, as antioxidants capable of protecting cells, tissues, organs, and whole organisms against the deleterious effects of harmful oxygen-derived species generated during oxidative stress.

Mitchell et al. teach methods of treating reperfusion injury such as myocardial infarction, comprising administering a reperfusion protectant effective in treating certain cardiovascular phenomena, including myocardial infarction (col. 3, lines 5-10 and col. 5, lines 26-39).

To the extent that independent claims 1, 9, and 16 encompass methods of preventing the harmful effect of ischemia," instant claims 1-23 are construed to read on any method of treatment employing the administering of the instant claimed nitroxide compounds as the term “preventing” or “prophylactic” are construed to mean the absolute absence of ischemia.

Thus, claims 1-23 are deemed to be anticipated by Mithcell et al. because Mithcell et al. teach the identical nitroxide compound recited in instant claim 2.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

7 March 2008
/C. R./Examiner, Art Unit 1611

/Brian-Yong S Kwon/
Primary Examiner, Art Unit 1614